The present Amendment further adds new claims 38-41. Support for new claims 38, 40, and 41 can be found, at least, in canceled claims 11, 27 and 28, respectively. Support for new claim 39 can be found in the Specification, at least, on page 8, lines 12-24 and page 14, lines 32-33. Thus, no prohibited new matter is believed to have been added by these amendments.

Claims 12-18 and 35-41 are now presented for consideration.

II. RESPONSE TO RESTRICTION REQUIREMENT

A. Restriction

In response to the outstanding Restriction Requirement, Applicants elect **with traverse Group II** drawn to a method of using the peptides of formula (I) to inhibit polymerization of amyloid β peptide. Applicants submit that elected Group II corresponds, at least, to amended **claims 12-18 and 38-41**. For example, claims 12-18, 38, and 40-41 (*i.e.*, former claims 11-18, 27, 28, 32, and 34 of Group II) are drawn to methods of using peptides of formula (I) to inhibit polymerization of amyloid β peptide. Also, **claim 39** (*i.e.*, former claim 33 of Group II) is drawn to methods of treating Alzheimer's disease. Applicants further submit that amended **claims 35-37**, which correspond to Groups VII-IX, respectively, should also be examined together with the claims of elected Group II for the reasons noted herein below.

Applicants respectively traverse the Restriction Requirement for at least the following reasons, and submit that claims 12-18 and 35-41 should be examined together.

First, with respect to groups II, III, VII, VIII, and IX, Applicants respectfully submit that Unity of Invention (*i.e.*, the specific compounds of Formula (I) that inhibit

polymerization of the amyloid peptide) **exists** between these groups. In this regard, the specific compounds of Formula I, which are capable of inhibiting polymerization of the amyloid peptide, are the unitary invention. These specific compounds of Formula I are also the common core structure between the compounds encompassed by the claims.

Second, it is respectfully submitted that groups II, III, VII, VIII, and IX, all pertain to the same class and subclass and therefore, would not impose a serious burden on the Examiner to examine all these groups. In addition, the claims should be examined together as they are all directed to compounds having the same inhibitory activity. Indeed, the search for such claims should be substantially, if not entirely, coextensive.

Under statute, an application may properly be required to be restricted to one of two or more claimed inventions only if they are able to support separate patents and they are either independent or distinct. See M.P.E.P. § 806.04 to § 806.04(j) (independent); see also M.P.E.P. § 806.05 to § 806.05(i)). Moreover, according to the M.P.E.P., there are two criteria for proper requirement for restriction between patentably distinct inventions:

> 1) The invention must be **independent** (M.P.E.P. § 802.01, § 806.04 and § 808.01) or **distinct** as claimed (M.P.E.P. § 806.05 to § 806.05(I)); **and**
>
> 2) There must be a **serious burden** on the Examiner if restriction is not required (M.P.E.P. § 803.02, § 806.04(a to j) and § 808.01(a) and § 808.02)).

These two criteria must **both** be met for the restriction requirement to be proper. Applicants believe that searching and examining the invention as now defined in claims 12-18 and 35-41, corresponding to groups II, III, VII, VIII and IX, **would not cause a serious burden** on the Examiner. No *prima facie* case regarding a serious burden on the Examiner has been shown by appropriate explanation of separate classification or separate status in

the art or different field of search (the subject matter of the claims are all classified in class 514, subclass 02+), as defined in M.P.E.P. §808.02. Thus, it is believed that no serious burden is imposed on the Examiner for searching these inventions. Therefore, one of the two requirements for a proper restriction is not met.

Therefore, Applicants respectfully request withdrawal of the Restriction Requirement and examination on the merits of claims 12-18 and 35-41 as hereby amended.

B. Species Requirement

The Examiner further requires that a species be elected prior to a search on the merits. Applicants elect **with traverse** SEQ. ID. NO. 8 (HHQKLVFF). Claims 13, 14, 18, and 35-41, as hereby amended, are readable on the elected species. Applicants elect the species with the understanding that the election is for search purposes only and that, should the examiner find the species to be patentable over the prior art, the examiner will extend the search to the remaining subject matter defined in the claims.

CONCLUSION

From the foregoing, further and favorable action in the form of a Notice of Allowance is respectfully requested and such action is earnestly solicited.

In the event that there are any questions concerning this amendment or the application in general, the Examiner is respectfully requested to telephone the undersigned so that prosecution of the application may be expedited.

Respectfully submitted,

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Date: December 2, 2002

ATTACHMENT
- Marked-up Copy of Amended Claims 12-18 and 35-37 -

12. (Amended) [Use according to Claim 11] The method of claim 38, wherein all the amino acids of the compound are D-isomers.

13. (Amended) [Use according to Claim 9] The method of claim 38, wherein Y' is Lys.

14. (Amended) [Use according to Claim 13] The method of claim 38, wherein Y' is Lys and Z' is Phe.

15. (Amended) [Use according to Claim 11] The method of claim 38, wherein Y' is Phe.

16. (Amended) [Use according to Claim 11] The method of claim 38, wherein X' is Val-Val.

17. (Amended) [Use according to Claim 11] The method of claim 38, wherein R_1 is acetyl.

18. (Amended) [Use according to Claim 11] The method of claim 38, wherein R_1 is H or R_2 is H.

ATTACHMENT
- Marked-up Copy of Amended Claims 12-18 and 35-37 -

35. (Amended) A method for treating or preventing demens in a [patients] patient having Downs syndrome comprising administering to the patient in need thereof an effective amount of a compound according to [Claim 1] formula

R_1-A' - Y' - Leu - X' - Z' - B' - R_2 (I)

in which X' means any group or amino acid imparting to the compound of formula (I) the ability to bind to the KLVFF-sequence in β amyloid peptide, or two amino acids imparting the same ability, but with the proviso that one is not proline;

Y' means any amino acid;

Z' means any non-acidic amino acid;

A' means a direct bond or an α-amino acid bonded at the carboxyl terminal of the α-carboxy group or a di-, tri-, tetra- or pentapeptide bonded at the carboxyl terminal of the α-carboxy group;

B' means a direct bond or an α-amino acid bonded at the α-nitrogen or a di-, tri-, tetra- or pentapeptide bonded at the α-nitrogen of the N-terminal α-amino acid;

R_1 is H or -CO-R_3 bonded at the α-amino group of A';

R_2 is H, -OR_4 or NR_5R_6 all bound to the α-carboxyl group of the α-carboxyterminal of B';

R_3 is a straight or branched carbon chain of 1-4 carbon atoms;

R_4 is a straight or branched carbon chain of 1-4 carbon atoms;

R_5 and R_6 independently are H, alkyl, cycloalkyl, aryl or substituted aryl or together are -$(CH_2)_n$-, where n is 4-5;

R_1 and R_2 together can form a hydrocarbon ring or heterocyclic ring; and

all the α-amino acids can be either D- or L-isomers.

ATTACHMENT
- Marked-up Copy of Amended Claims 12-18 and 35-37 -

36. (Amended) A method for treating or preventing hereditary cerebral hemorrhage associated with amyloidosis (Dutch type) comprising administering to a patient in need thereof an effective amount of a compound according to [Claim 1] formula

$$R_1\text{-}A' - Y' - Leu - X' - Z' - B' - R_2 \quad (I)$$

in which

X' means any group or amino acid imparting to the compound of formula (I) the ability to bind to the KLVFF-sequence in amyloid β peptide, or two amino acids imparting the same ability, but with the proviso that one is not proline;

Y' means any amino acid;

Z' means any non-acidic amino acid;

A' means a direct bond or an α-amino acid bonded at the carboxyl terminal of the α-carboxy group or a di-, tri-, tetra- or pentapeptide bonded at the carboxyl terminal of the α-carboxy group;

B' means a direct bond or an α-amino acid bonded at the α-nitrogen or a di-, tri-, tetra- or pentapeptide bonded at the α-nitrogen of the N-terminal α-amino acid;

R_1 is H or -CO-R_3 bonded at the α-amino group of A';

R_2 is H, -OR_4 or NR_5R_6 all bound to the α-carboxyl group of the α-carboxyterminal of B';

R_3 is a straight or branched carbon chain of 1-4 carbon atoms;

R_4 is a straight or branched carbon chain of 1-4 carbon atoms;

R_5 and R_6 independently are H, alkyl, cycloalkyl, aryl or substituted aryl or together are $-(CH_2)_n-$, where n is 4-5;

R_1 and R_2 together can form a hydrocarbon ring or heterocyclic ring; and

all the α-amino acids can be either D- or L-isomers.

ATTACHMENT
- Marked-up Copy of Amended Claims 12-18 and 35-37 -

37. (Amended) A method for preventing [fribal] fibril formation of human amyloid protein in a patient in need [of such prevention] thereof comprising administering to said patient an effective amount of a compound according to [Claim 1] formula

$$R_1\text{-}A' - Y' - Leu - X' - Z' - B' - R_2 \quad (I)$$

in which

X' means any group or amino acid imparting to the compound of formula (I) the ability to bind to the KLVFF-sequence in amyloid β peptide, or two amino acids imparting the same ability, but with the proviso that one is not proline;

Y' means any amino acid;

Z' means any non-acidic amino acid;

A' means a direct bond or an α-amino acid bonded at the carboxyl terminal of the α-carboxy group or a di-, tri-, tetra- or pentapeptide bonded at the carboxyl terminal of the α-carboxy group;

B' means a direct bond or an α-amino acid bonded at the α-nitrogen or a di-, tri-, tetra- or pentapeptide bonded at the α-nitrogen of the N-terminal α-amino acid;

R_1 is H or $-CO-R_3$ bonded at the α-amino group of A';

R_2 is H, $-OR_4$ or NR_5R_6 all bound to the α-carboxyl group of the α-carboxyterminal of B';

R_3 is a straight or branched carbon chain of 1-4 carbon atoms;

R_4 is a straight or branched carbon chain of 1-4 carbon atoms;

R_5 and R_6 independently are H, alkyl, cycloalkyl, aryl or substituted aryl or together are $-(CH_2)_n-$, where n is 4-5;

R_1 and R_2 together can form a hydrocarbon ring or heterocyclic ring; and

all the α-amino acids can be either D- or L-isomers.